REMARKS

Claims 76-116, 118-127 and 135-139 presently appear in this case. Claims 76-107 have been withdrawn from consideration. No claims have been allowed. The present communication is intended to supplement applicant's amendment of November 26, 2010, and is further responsive to the Official Action of May 26, 2010. Reconsideration and allowance of all of the claims now present in the case are respectfully urged.

In the remarks accompanying applicant's amendment of November, 26, 2010, it was explained why one of ordinary skill in the art would not find it obvious to use any of the conjugates of Jorgensen for the purpose of protein delivery. However, it is further requested that the examiner specifically consider claim 118 (as well as new claims 136 and 137 and withdrawn claim 93) and those claims dependent therefrom in their own right as these claims further define over Jorgensen. In claim 118, the structure of the polyalkylamine is specifically claimed. Note that R_4 is a (O)-NR_6R_7 group in which each of R_6 and R_7 may be a saturated or unsaturated branched or linear polyalkylamine. The formulas for typical compounds within the scope of claim 118 are set forth in figures 1A-1D of the present application. Claim 118

does not comprehend any of the therapeutic compounds of Jorgensen.

In order to understand what is actually disclosed by Jorgensen, it must be carefully analyzed. Paragraph [0014] of Jorgensen, and those paragraphs preceding it, indicate the background of the invention, i.e., the desirability of generating gene delivery systems with a balance between stability and activity. Paragraph [0015] states that Jorgensen's co-pending application teaches a system based on a modified lipid wherein the lipid carries a carbohydrate moiety. It states that these modified lipids have been found to be stable and to have low toxicity. They require the linking of an additional moiety to the lipid to assist in the provision of a modified lipid which is stable and has low toxicity. This paragraph concludes with the sentence, "There is a desire in the art to provide lipids comprising groups to which additional moieties may be readily linked." Paragraph [0016] then states that the Jorgensen invention is intended to alleviate the problems of the prior art, i.e., to provide conjugates to which additional moieties, such a carbohydrate moieties, may be readily linked for the purpose of making compounds that that will serve as delivery vehicles.

From this analysis, it becomes clear that the only delivery vehicles disclosed by Jorgensen are those which

include a modified lipid wherein the modification of the lipid is the presence of a carbohydrate moiety. These are referred to later in Jorgensen as "neoglycolipids." See Figure 3 and paragraph [0083] of Jorgensen. Note also that the experimental section of the examples is directed to "Synthesis of Neoglycolipids." Note further that the LMD formulations referred to in Figures 4 and 5 were tested for the stabilizing effects of the neoglycolipids of Jorgensen. Paragraph [0122] states that first the LMD were formulated and secondly a suspension of synthesized neoglycolipids was added to the LMD and incubated. Different percentages of all the neoglycolipids produced were tested for stabilization effect.

The lipid that is produced in accordance with Jorgensen to facilitate reaction with a carbohydrate moiety so as to obtain the desired end product is known as a "hydroxylamine lipid" or an "aminoxy lipid," such as that of lipid 11 of Figure 1, which is also shown in Figure 6. See paragraphs [0081] and [0086] of Jorgensen. Note that Jorgensen states in paragraph [0038], "We have found the provision of a lipid comprising an aminoxy group allows for simple linking of further moieties to the lipid via the aminoxy group."

Accordingly, it can be seen that the lipid 11 in Figure 1, which is also shown in Figure 6, is not intended for

therapy, but is intended as an intermediate used to make the neoglycolipids which are used in therapy. Similarly, the lipid 8 is merely an intermediate for making the hydroxylamine of lipid 11.

The polyalkylamine of Jorgensen is present as a linker. See paragraphs [0047] and [0113] of Jorgensen. Paragraph [0113] is particularly of interest where it states:

> Synthesis of Neoglycolipids: Each member of the targeted family of neoglycolipids consisted of a cholesterol bearing lipid and an oligosaccharide molecule bound together via a linker. The whole synthetic approach was divided in two parts; firstly, the synthesis of a lipid containing the linker and secondly the chemioselective coupling of this lipid with chosen sugar molecules. The key to this strategy is the formation of a hydroxylamine (FIG. 1).

The definition of sphingoid-polyalkylamine conjugate as set forth in claim 118 does not include conjugates with carbamoyl groups at both ends of the polyalkylamine chain. While the polyalkylamine is joined to the sphingoid by means of a carbamoyl group (R_3 and/or R_4), the polyalkylamine is not linked to anything at its free end. It is simply a saturated or unsaturated branched or linear polyalkylamine. This does not comprehend a polyalkylamine linked to a sugar molecule. Thus, the polyalkylamine of claim 118 is not a linking group, but is a freely extending polyalkylamine on the compound or a cyclic polyalkylamine.

The examiner states that it would be obvious to substitute ceramide for cholesterol in the conjugates of Jorgensen and use it therapeutically for delivering drugs. However, as discussed above, the only compounds used to deliver anything therapeutically in Jorgensen are the neoglycolipid compounds of Jorgensen. There would be no motivation for anyone of ordinary skill in the art to use any of the intermediate compounds used by Jorgensen to make the neoglycolipids, such as lipid 8 or lipid 11 of Figure 1, or any modifications thereof, to substitute ceramide for cholesterol. As claim 118 does not read on a neoglycolipid, it would not be obvious to combine such intermediates of Jorgensen with an immune response modulating biologically active molecule as is required in claim 118 and those claims dependent therefrom. Accordingly, reconsideration and withdrawal of the rejections of record are respectfully urged.

Claim 118 has now been amended in order to clarify the language thereof without changing the intended scope. One change is to specify that at least one of R_3 and/or R_4 comprises a said polyalkylamine. This amendment eliminates the possibility that all of R_3, R_6 and R_7 are hydrogen atoms. This is supported by page 10, line 10, of the specification, which states that the sphingoid polyalkylamine conjugate

includes at least one polyalkylamine chain. The language about R_3 being a hydrogen has also been clarified.

Applicant wishes to further point out that even if it were obvious to use the conjugates of Jorgensen or Miller to deliver protein (and this is not something that one of ordinary skill in the art would learn from either Jorgensen or Miller), the unexpected results of using such conjugates as a vaccine would overcome any *prima facie* case of obviousness. The present specification establishes that the conjugate of the present invention has adjuvant properties when administered with an immune response modulating biologically active molecule.

The present art rejections are not anticipation rejections but obviousness rejections. As stated in *In re Spormann*, 150 USPQ 449, 452 (CCPA 1966):

> The inherency of an advantage and its obviousness are entirely different questions. That which may be inherent is not necessarily known. Obviousness cannot be predicated on what is unknown.

Accordingly, claim 108 is also allowable because of the unexpected results reported for the first time in the present specification. The inherency of these results were not known and thus could not have been obvious.

While claim 108 is allowable for the reasons discussed previously in view of the fact that Jorgensen does

not disclose delivering anything but genes and claim 108 does not comprehend genes, as well as the additional reasons discussed in the previous paragraph, it is requested that the examiner specifically reconsider the rejection with respect to claim 118 and those claims dependent thereon in view of the fact that the therapeutic compounds of Jorgensen do not fall within the scope of the structural formula of claim 118. The examiner should also particularly consider the preferred conjugate of the present invention, which is CCS as claimed at claim 115 and which does not fall within the scope of anything disclosed in Jorgensen as being a delivery agent.

Accordingly, consideration of the present supplemental amendment in conjunction with applicant's amendment of November 26, 2010, is earnestly solicited.

Respectfully submitted,

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